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properties not taught or suggested by U.S. Patent No. 5,198,540. As described in the specification (see, e.g., page 7, lines 25-27), use of the LPCs of the instant application and claims in solution phase biopolymer synthesis provides biopolymers of higher yield and purity than those taught in the cited reference.

Specifically, as described in Example 7 of the instant specification, use of a trivalent LPC of the instant claims, dT<sub>3</sub>-Aryl-LPC, in solution phase oligonucleotide synthesis provides the desired 10-mer in an overall yield of 33%. The cited reference teaches, in Table 1, use of the divalent LPCs taught therein in oligonucleotide synthesis to afford the a 5-mer, 6-mer and a 7-mer in overall yields of 14%, 8% and 5%.

The increase in yield obtained using the multivalent LPCs (*i.e.*, those possessing 3 to 6 points of attachment) of the instant application is neither taught nor suggested by the cited reference, which teaches use of divalent LPCs. The cited reference would not have provided one of ordinary skill in the art motivation to have prepared and tested the LPCs of the instant claims. Nor does the cited reference teach or suggest the structural modifications required to achieve the above-noted increase in solution phase biopolymer synthesis yield. Therefore, the instant claims are not obvious over the teachings of U.S. Patent No. 5,198,540.

## The Declaration of Köster

Provided herewith is an executed DECLARATION of KÖSTER demonstrating the increase in solution phase biopolymer synthesis yield achieved with the LPCs of the instant claims versus the results provided in U.S. Patent No. 5,198,540 for solution phase biopolymer synthesis using the divalent LPCs taught therein. As shown in EXAMPLE 7 of the instant specification and in the DECLARATION, use of an LPC of the instant claims possessing 3 points of attachment (1,3,5-tris[9-(2'-deoxythymidin-3'-O-yl)-2,5-diaza-1,6,9-trioxononyl]-benzene (dT<sub>3</sub>-Aryl-LPC)) in solution phase oligonucleotide synthesis provides an

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increased yield of the desired product as compared to solution phase oligonucleotide synthesis using the following LPC of the cited reference, which possesses two points of attachment:

OMe
$$CI-C$$
OC(O)-(CH<sub>2</sub>)<sub>6</sub>-C(O)O
OMe
$$OMe$$

Specifically, use of the LPC of the instant claims provides a 10-mer oligonucleotide in an overall yield of 33%, as compared to overall yields of a 5-mer, 6-mer and a 7-mer of 14%, 8% and 5% using the LPC of the cited reference. The structural modifications required to achieve this increase in yield are not taught or suggested by the cited reference. Therefore, the instant claims are not obvious over the teachings of U.S. Patent No. 5,198,540.

Applicant respectfully requests reconsideration and withdrawal of this rejection.

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\* \* \*

In view of the above, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

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By:

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## IN THE UNITED TATES PATENT AND TRADEMARK OFFICE

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KÖSTER et al.

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SYNTHESIS

Art Unit:

1623

Examiner:

Wilson, J.

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## ATTACHMENTS TO SUPPLEMENTAL RESPONSE TO OFFICE ACTION

The following attachments are provided:

(1) An executed DECLARATION of KÖSTER.